



Bilirubin metabolism and Jaundice-1

By

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INTENDED LEARNING OBJECTIVES (ILOs)



By the end of this lecture the student will be able to:

- 1. Demonstrate the steps of heme catabolism**
- 2. Distinguish different types of jaundice**

Outlines

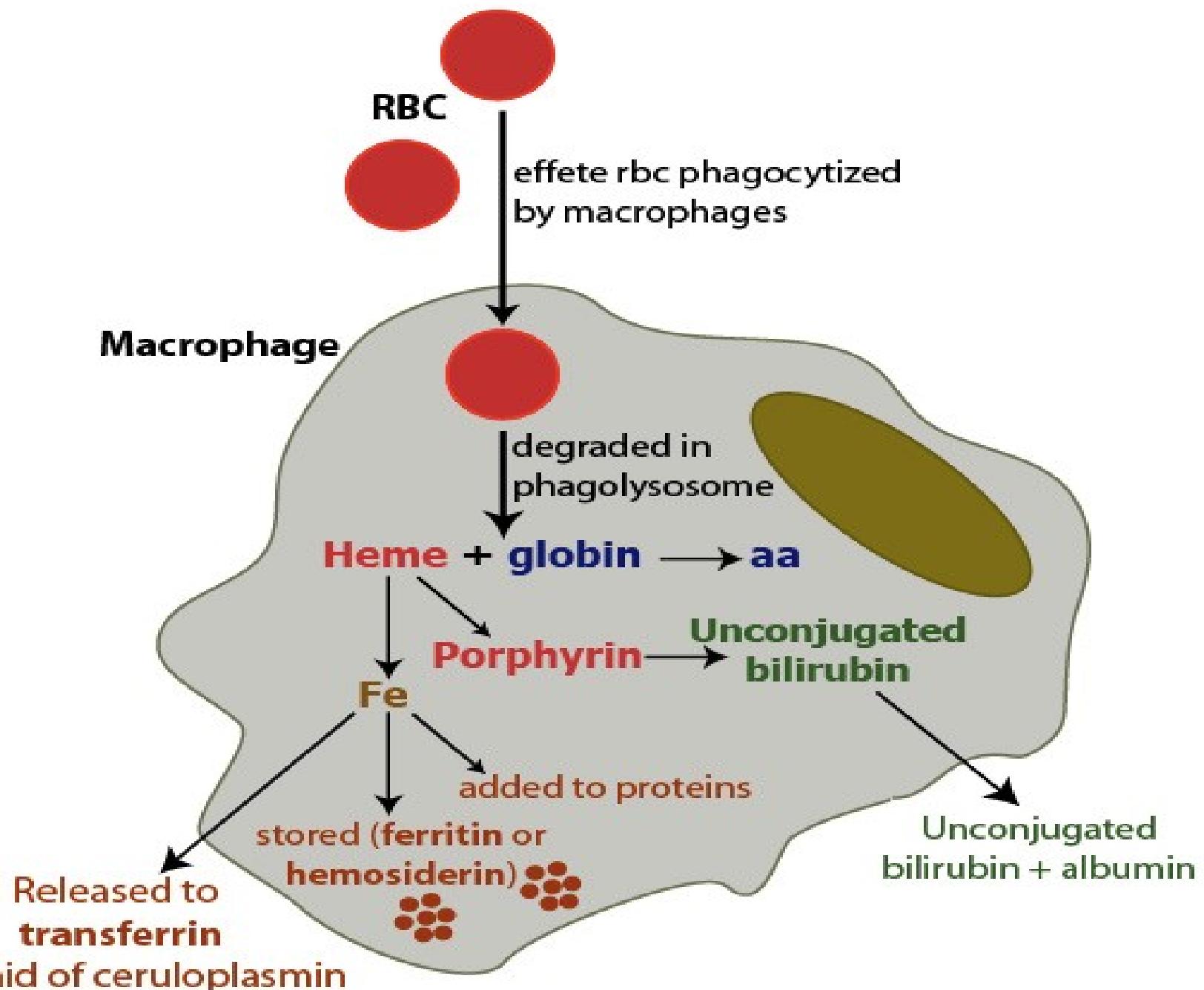
What are the steps of heme catabolism

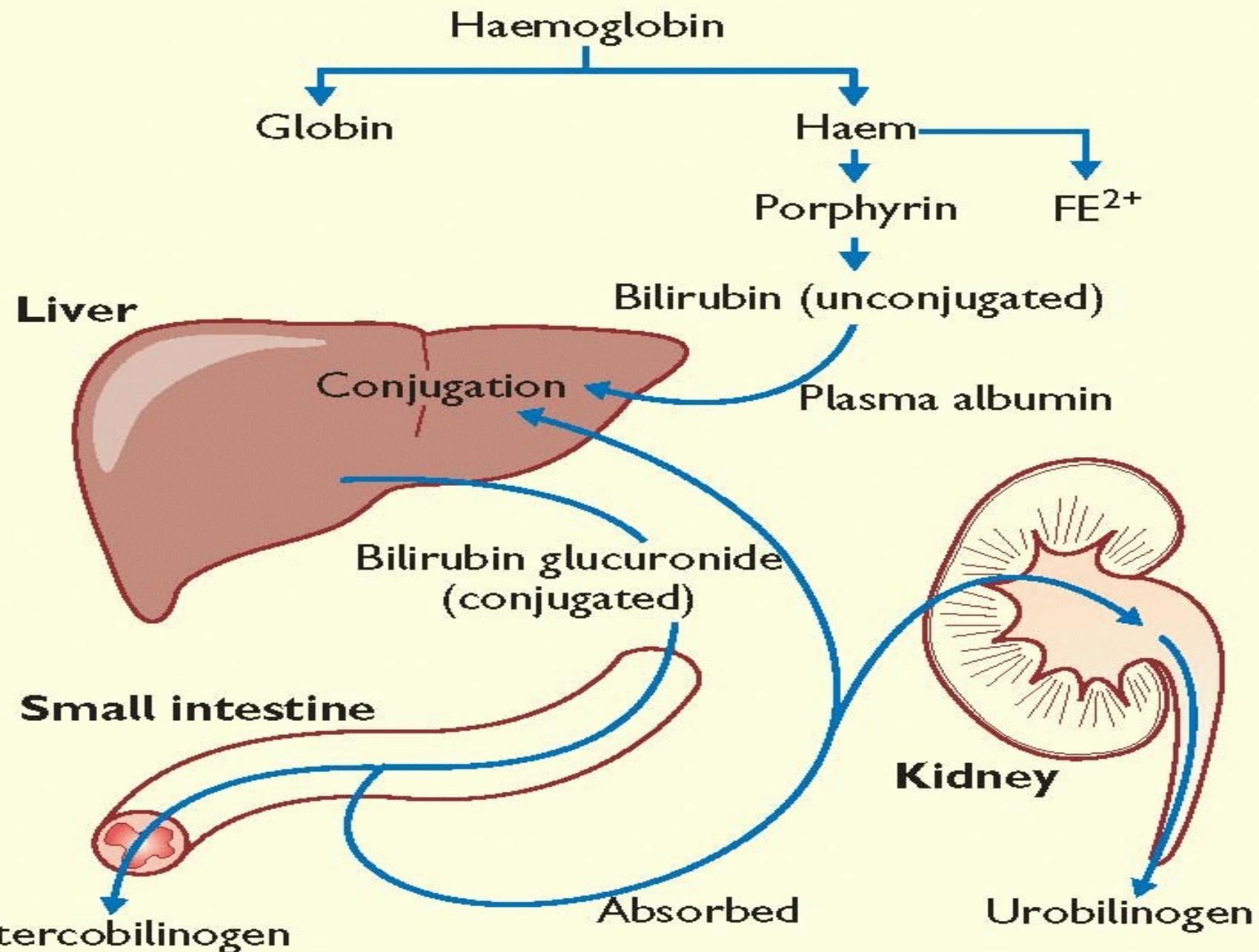
?What is Jaundice

Catabolism of Heme

Human adults normally destroy about **200 billion erythrocytes per day.**

After RBCs reach the end of their life span (average **120 days), they are phagocytosed by **reticulo-endothelial cells** of liver, spleen and bone marrow.**





?What are the steps of heme catabolism

Steps of Heme catabolism

**Formation of .1
bilirubin**

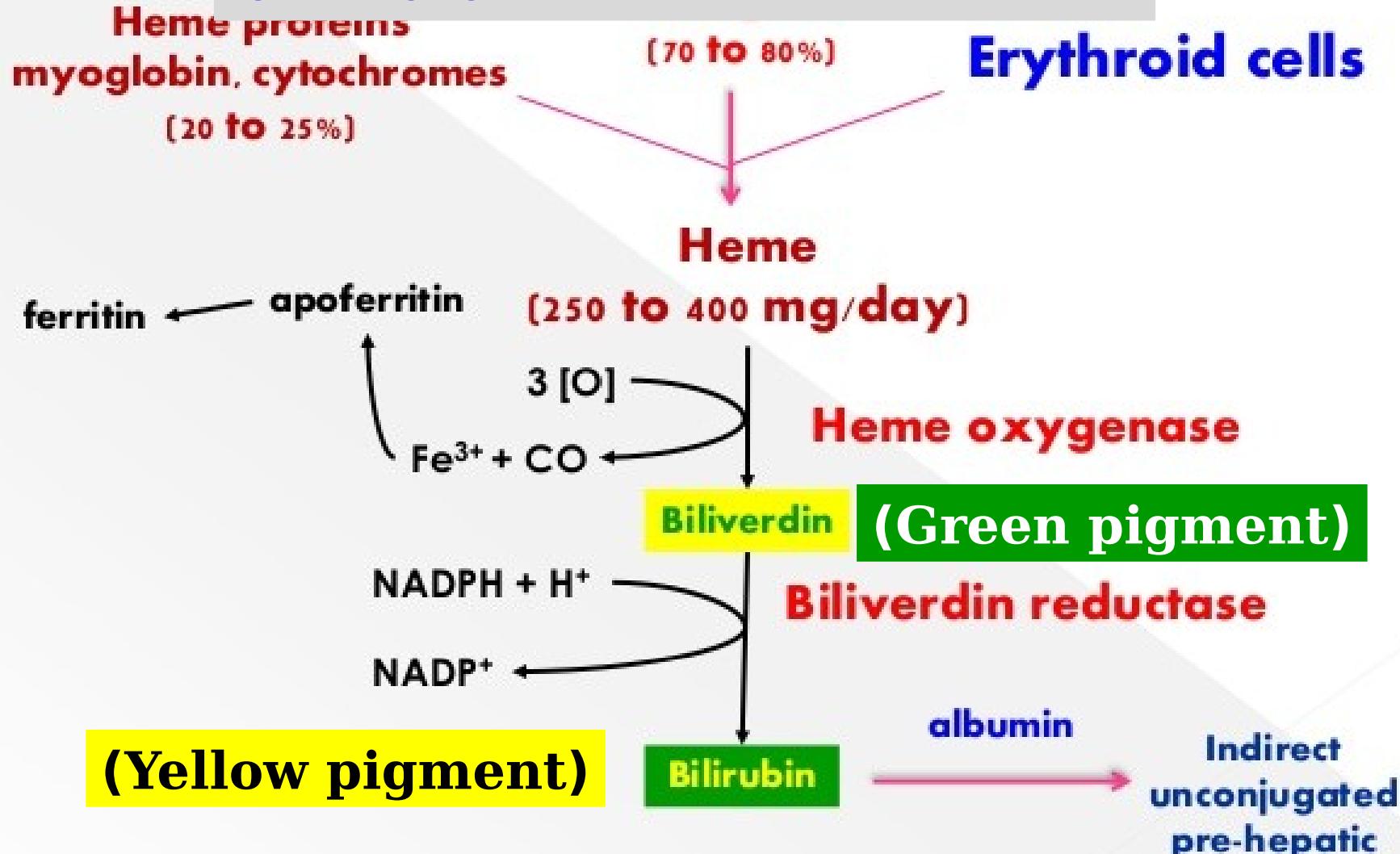
**Uptake of bilirubin by the .2
liver**

Formation of bilirubin diglucuronide .3

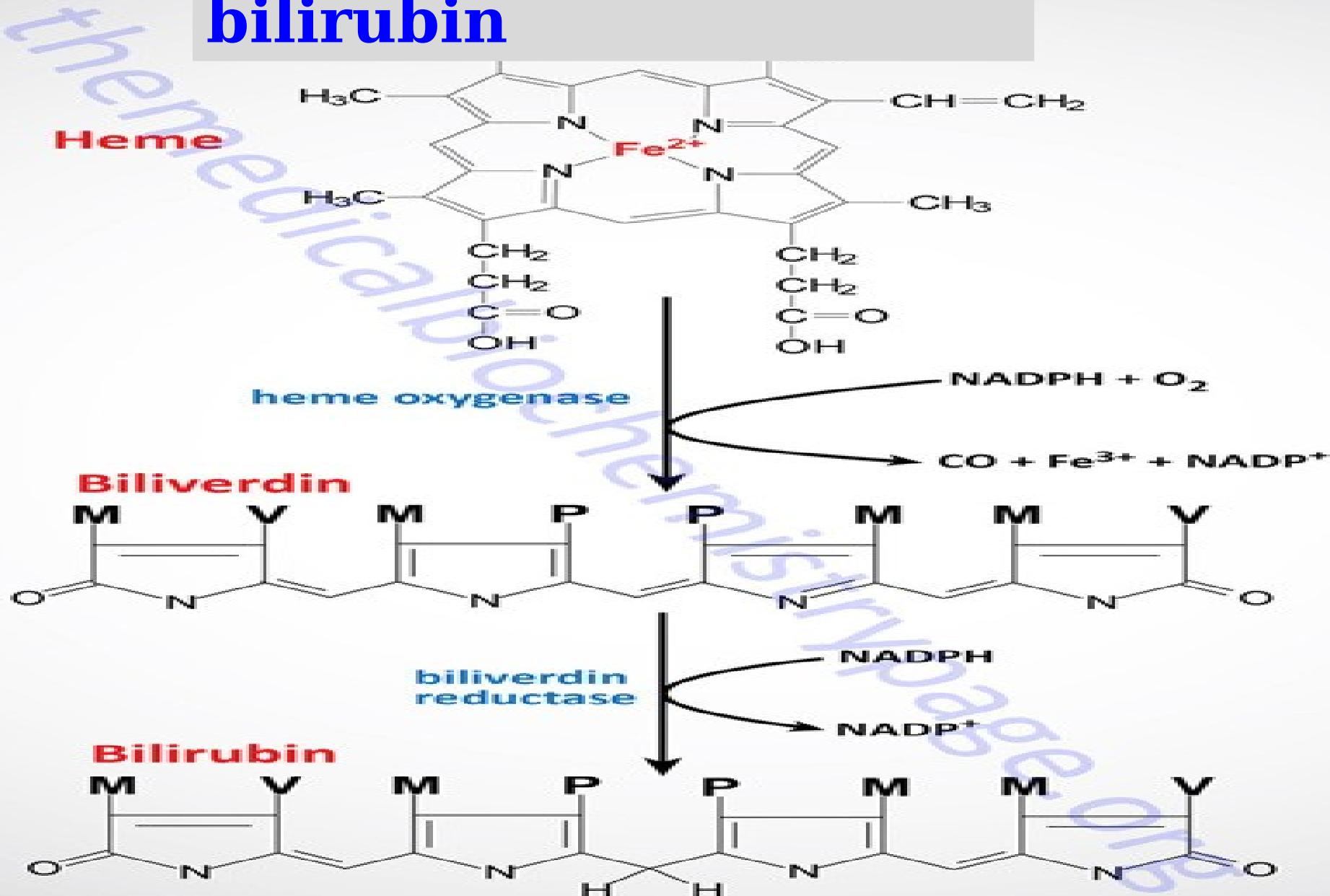
Secretion of bilirubin into bile .4

Formation of urobilins in the intestine .5

Formation of bilirubin

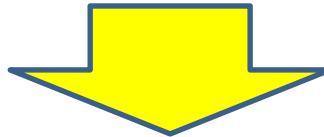


Formation of Bilirubin



Formation of .1 bilirubin

Heme catabolism is carried out in the microsomal heme oxygenase system of the reticuloendothelial cells



**Opening of the porphyrin ring
converting cyclic heme to linear biliverdin
(green pigment)**



Formation of bilirubin



Iron is liberated from heme



In mammals, biliverdin is further reduced to bilirubin (yellow pigment) by NADPH - dependent biliverdin reductase enzyme

Uptake of bilirubin by the liver

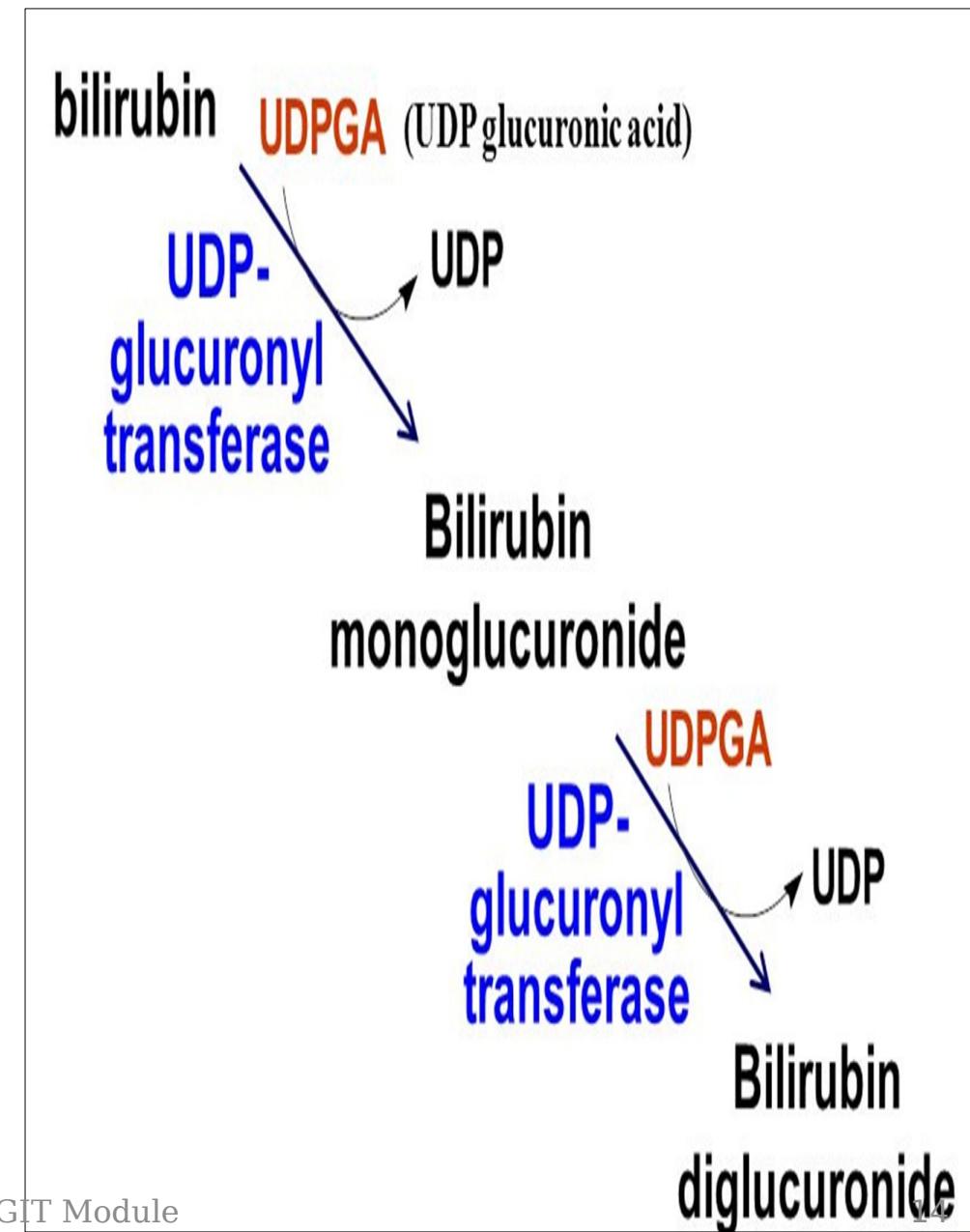
Bilirubin is slightly soluble in plasma. It transported to the liver bound to albumin forming unconjugated or indirect bilirubin

Liver uptake bilirubin by carrier mediated transport (facilitated transport)

Formation of bilirubin diglucuronide .3

Bilirubin
is converted to a
more polar
molecule by
conjugation with
two molecules of
glucuronic acid

This reaction is
catalyzed by
glucuronosyl
transferase
enzyme



Secretion of bilirubin into bile .4

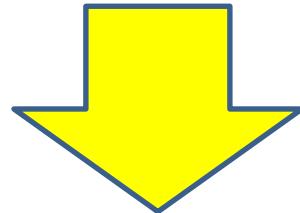
Bilirubin diglucuronide (conjugated bilirubin)

is actively transported against concentration gradient into the bile

Mostly, it is rate-limiting step for the entire process of hepatic bilirubin metabolism

Formation of urobilins in the intestine .5

Conjugated bilirubin is **hydrolyzed** and **reduced** by bacteria in the gut giving **urobilinogen**



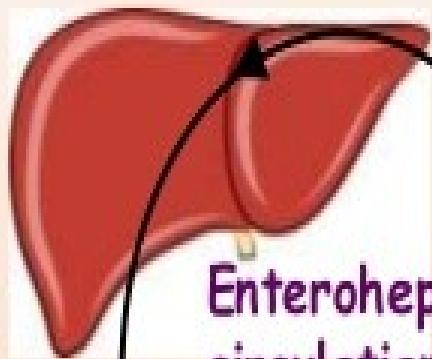
Most of the urobilinogen is **oxidized** by intestinal bacteria to **stercobilin**, which gives **feces** the characteristic **brown** color

Formation of urobilins in the intestine .5

Some of the urobilinogen is reabsorbed from the gut and enters the portal blood and then resecreted into the bile

The rest of the urobilinogen is transported by the blood to the kidney, where it is converted to yellow urobilin and excreted, giving urine its characteristic color

Bilirubin diglucuronide



Systemic Circulation

Urobilinogen

Oxidised 4 mg/day

Urobilin

Deconjugation

Glucuronidase

Bacterial enzymes

100 - 200 mg/day

Bilirubin diglucuronide

Bilirubin

Urobilinogen

Stercobilinogen

Oxidised
Stercobilin

20%

Excreted in Urine

Yellow color of urine

Excreted - BROWN color of Feces



?What is Jaundice



JAUNDICE

What is jaundice (icterus)



yellow color of skin, nail beds, and sclerae due by deposition of **bilirubin**, secondary to **hyper-bilirubinemia**

The normal plasma bilirubin level range from 0.3 - 1.2 mg/dl .

If the serum bilirubin exceeds 1 mg/dl
→ **hyperbilirubinemia**

If the bilirubin level exceeds 2 mg/dl, **Jaundice will occur**





Note: The sclera is particularly affected because it is rich in elastin, which has a high affinity for bilirubin



Note: unconjugated bilirubin can cross the blood-brain barrier into the central nervous system causing so encephalopathy .(kernicterus)

Alternatively, because of its water-solubility, only conjugated bilirubin can appear in urine



:Note: Choluric jaundice

Choluria is the presence of bile pigments in the urine and occurs only in **conjugated** hyperbilirubinemia

:Acholuric jaundice

Is the absence of bile pigments in the urine and occurs only in **unconjugated** hyperbilirubinemia

MCQ

The substance deposited in skin and sclera in jaundice is:

- A. Biliverdin.
- B. Only unconjugated bilirubin.
- C. Only direct bilirubin.
- D. Both bilirubin and bilirubin diglucuronide.
- E. Hematin.

Summary

- After RBCs reach the end of their life span (average 120 days), they are phagocytosed by reticulo-endothelial cells of liver, spleen and bone marrow.
- Bilirubin is the end product of heme catabolism
- Jaundice is yellow color of skin, nail beds, and sclerae due by deposition of bilirubin, secondary to hyperbilirubinemia

Thank
you



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